REMARKS

Initially, Applicant's attorney wishes to thank Examiner Kim for the careful consideration given this application. Applicant's attorney acknowledges the caseload of Examiner Jones and feels very comfortable dealing with Examiner Kim. It should be noted, however, that both Examiner Kim and Criares suggested filing this case as an RCE and directing it to Examiner Jones' attention, due to his familiarity with the related art.

Initially, the Examiner objected to the amendment filed October 18, 1999, under 35 U.S.C.§132 because it reportedly introduces new matter into the disclosure. Similarly, claims 20, 21, 23-26 have been rejected under 35 U.S.C.§112 due to their inclusion of atorvastatin and cerivastatin in these claims. The Examiner has stated that these two species should be removed from the specification and cancelled from the claims because they purportedly introduce new matter. It is respectfully submitted that the objection under 35 USC§132 and the rejection under 35 USC§112 are inappropriate both procedurally and substantively. This same subject matter has been present in the claims for over three years, through numerous communications with the Office, specifically discussed during an interview, and reintroduced in an RCE which the Examiner suggested Applicant file. To raise this issue at this relatively late stage of prosecution is the exact type of piecemeal examination prohibited by §707.07(g) of the MPEP. Even *assuming arguendo* that the current position of the Examiner is procedurally proper, it is respectfully submitted that amendments do not introduce new matter. Rather, these amendments are being made simply to clarify the present claims. The Courts have consistently held that new language is not ipso facto new matter. For example, it has been held that the introduction of "for example, polyvinylchloride" to clarify the term "castenable residenous material" was not the addition of new matter to the specification.[1] As the Examiner is well aware, Applicant is not required to teach that which is well known in the art but is rather encouraged to limit the disclosure to that which is necessary to practice and understand the invention. It is respectfully submitted that the amendments submitted October 18, 1999 should be granted the benefit of the priority date claimed because all that is required is that each claim limitation be present expressly

[1] Chem Case Corp. v. Arco Industries (5 USPQ 2nd 1225)

implicated, or inherently supported in the original filed disclosure. As Applicant states in the specification, "L-arginine may be used in conjunction with virtually any of the family of those substances known as HmG-CoA reductase inhibitors" (page 9, lines 13-14). The specific list of the inhibitors of HmG-CoA reductase were "by way of example only" and atorvastatin and cerivastatin were both implicitly and inherently disclosed in the application as originally filed. In fact, atorvastatin (also known as Lipitor™) was approved by the FDA on December 16, 1996 and cerivastatin was approved by the FDA on June 3, 1997. Copies of representative Orange Book listing are provided herewith evidencing that both of these were well known. Also illustrated in the Orange Book listing are the Patent data covering each of the respective compounds. Clearly, both of these compounds were well known at the time of filing.

This issue of "new matter" impacts the art rejections made by the Examiner under 35 U.S.C.§102(e). Simply put, if the limitations discussed above are given proper priority the Liao et al reference is not prior art under 35 U.S.C.§102(e). **Even if the Examiner maintains her position on the priority date, the rejection of claims 20, 21, and 23-26 would be inappropriate because the present claims are not anticipated by U.S. Patent No. 6,147,109 by Liao et al.** Initially, even if the Examiner maintains the new matter rejection, it is clear that Applicant's original disclosure predates the filing date of U.S. Patent No. 6,147,109 to Liao. Although Applicant's attorney believes it is unnecessary to file a Rule 131 Affidavit at this point due to the issue regarding 35 USC §120, it is respectfully submitted that an Affidavit under Rule 131 would simply reiterate that which is clearly stated in the application. Namely that the disclosure of Hmg-CoA reductase inhibitors and the necitation of "L-arginine being used in "conjunction with virtually any of the family of those substances known as Hmg-CoA reductase inhibitors" (page 9, lines 13-14) clearly supports an earlier filing date than Liao. This statement in affidavit form would remove the Liao reference from being cited against the present application as cerivastatin and atorvastatin were known Hmg-CoA reductase inhibitors. If the Examiner insists that new matter has been added to the specification and the claims, it is respectfully requested that the Examiner provide comment on whether she would favorably receive an Affidavit under Rule 131 using the prior patent as clear evidence of prior conception and reduction to practice.

Claims 1, 2, 5, 6, 12, 13, 16 and 17 have been rejected under 35 U.S.C.§103(a) as being obvious over Morris et al.(1994). It is respectfully submitted that this reference has been previously addressed in the parent application and been found to not anticipate nor make obvious claims of similar scope to those being presented herein. In particular, Morris' teaching of an obscure Hmg-CoA reductase inhibitor arginine salt, without any suggestion, motivation or otherwise rationale for using it to treat a disease state in no way anticipates or makes obvious the present invention. Initially, the Examiner is directed to the fact that claims 1, 2, 5, 6 and 16 and 17 are method claims and that all of the limitations recited therein (i.e. "treating a disease") should be read into the claim. Additionally, the preamble of therapeutic composition claims 12 and 13 breaths life and meaning into these claims, and therefore Morris does not even impact claims 12 and 13. Accordingly, the rejection should be withdrawn.

Claims 1-6, 12, 13, 16-19 and 22 stand rejected under 35 U.S.C.§103(a) as being unpatentable over U.S. Patent No. 5,634,895 to McGovern et al. and U.S. Patent No. 5,634,895 to Igo et al. The Examiner seems to be repeating the objection previously presented and addressed. As the Examiner points out, the claims do differ in claiming combinations of L-arginine and Hmg-CoA reductase inhibitors. The Examiner also states, however, that it "would have been obvious because all of the components are well known individually for treating restenosis following angioplasty". To rebut Applicant's previously submitted arguments regarding McGovern and Igo, the Examiner states that "regardless of the purposes of the mechanism of the action of each of the active agents, . . . the ultimate effect is the same." This statement is inconsistent with the Examiner's burden of establishing a prima facie case of obviousness and the case cited. The case law only supports a prima facie case of obviousness when a combination of elements were known for the same purpose. The Examiner has shown no suggestion of motivation to combine the elements, and no reasonable expectation of success. The Examiner's reliance on this case law is misplaced. To the extent that the case law applies, it requires that the two elements have the same purpose, not the same end result as stated by the Examiner. As was pointed out previously, L-arginine and pravastatin as described in McGovern and Igo are not used for the same purpose and the idea of combining them would not flow logically from their individual teachings. The Examiner further states, with regard to claims 16

and 17 that a method of stimulating NO acting agents involves a mechanism of action which is inherent in the treatment of medical disease conditions. It is respectfully pointed out to the Examiner that any use of inherency is limited by the recognized utility of the agent by the prior art. The utility of these two agents was not recognized. As is clearly as is demonstrated by the numerous patents that have been issued to Applicant and others in this field, the utility that has been described and claimed by Applicant was not known in the prior art.

Only through Applicant's teaching is one motivated to administer both L-arginine and an agent that enhances NO production (e.g., via enhanced conversion of L-arginine into NO). The Federal Circuit has consistently held that in order to establish a proper prima facie case of obviousness, the PTO must show a motivation apart from the teaching of the invention to combine the references. Since neither reference suggests or teaches a reason for the combination of either agent with the other, it is respectfully submitted that a prima facie case of obviousness has not been established.[2] There is no suggestion in McGovern that there would be any benefit or advantage gained by combining a Hmg-CoA reductase inhibitor and L-arginine. Nor is there any suggestion or teaching in Igo that L-arginine would provide any added benefit to a Hmg-CoA reductase inhibitor formulation. Accordingly, the rejection should be withdrawn.

The Examiner also rejected claims 2, 5, 6 and 19 under 35 U.S.C.§103(a) as being obvious since they are within the knowledge of the skilled pharmacologist and conventional routes of administration. These dependent claims should be allowed based upon their dependency on the claims presented above that are in condition for allowance.

Finally, the Examiner has rejected claims 1, 2, 5, 12, 13, 20, 21 and 24-26 under 35 U.S.C.§103(a) for being obvious over Wang et al. (1994), Pharmacol. Res. (1996) and U.S. Patent No. 6,093,719 to Bocan. The stated basis for the obviousness rejection of claims provided in the Office Action is that Wang purportedly teaches that dietary L-arginine prevents atherogenesis in the coronary artery of the hypercholesterolemic rabbits. The Examiner states that the U reference teaches that cerivistatin interferes with a major process involved in

[2] The Federal Circuit, in, *In re Rouffe* reversed an obviousness rejection where, as in this case, the Examiner improperly pieced together elements in the prior art when there was not motivation to do so. 47 USPQ2d 1453, 1457-1458 (Fed. Cir. 1998).

atherogenesis and Bocan teaches that atorvastatin alone results in a less atherogenic lipoprotein profile. In the opinion of the Examiner, "combinations of L-arginine and cerivistatin or atorvastatin to treat a condition such as atherogenesis would have been obvious because all of the components are well known individually for treating atherogenesis." Applicant respectfully disagrees for the reasons discussed above.

As presented in the arguments above, it is respectfully asserted that the purpose provided in the art of administering a Hmg-CoA reductase inhibitor (i.e., atorvastatin) is to reduce serum cholesterol to thereby reduce platlet aggregation (see e.g., column 2, lines 46-51 of Bocan), and the purpose of administering L-arginine is to form NO thereby reducing vasoconstriction (see e.g., abstract of Wang). Accordingly, even assuming arguendo that cerivistatin, atorvastatin, and L-arginine are described in the art as set forth by the Examiner, these teachings do not satisfy a prima facie case of obviousness. The two claimed elements (e.g., L-arginine and cerivistatin / atorvastatin) are not used for the same purpose, and the idea of combining them would not flow logically from the individual teachings.

Furthermore, neither Wang nor Bocan provides any motivation to combine L-arginine and a Hmg-CoA reductase inhibitor. Absent such motivation or suggestion, it is improper to combine the references in support of an obviousness rejection under 35 U.S.C.§103. See the discussion above. Bocan is directed towards a method of treatment of atherosclerosis, which will restore endogenous vascular endothelium-dependent activities. Again, Bocan fails to recognize any role that an Hmg-CoA reductase inhibitor plays in activation of NOS to result in vasodilation.

CONCLUSION

In conclusion, it is respectfully requested that the Examiner specifically address the issues presented in this application and pass this case to issue. In view of the remarks presented above, it is believed that pending claims 1-6, 12, 13 and 16-22 are in condition for allowance and notice to such effect is respectfully requested. Should the Examiner have any questions regarding the above, the Examiner is invited to contact the undersigned at her convenience.

Respectfully submitted,

PEPPER HAMILTON LLP

Raymond A. Miller
Registration No. 42,891

Date: April 7, 2003
Pepper Hamilton LLP
One Mellon Center, 50th Floor
500 Grant Street
Pittsburgh, PA 15219
Tel.: (412) 454-5023
Facsimile: (412) 281-0717

Proprietary Name Search Results from "Rx" table for query on "lipitor."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
020702		No	ATORVASTATIN CALCIUM	Tablet; Oral	EQ 10MG BASE	LIPITOR	PFIZER
020702		No	ATORVASTATIN CALCIUM	Tablet; Oral	EQ 20MG BASE	LIPITOR	PFIZER
020702		No	ATORVASTATIN CALCIUM	Tablet; Oral	EQ 40MG BASE	LIPITOR	PFIZER
020702		Yes	ATORVASTATIN CALCIUM	Tablet; Oral	EQ 80MG BASE	LIPITOR	PFIZER

Thank you for searching the Electronic Orange Book

Return to Electronic Orange Book Home Page

Proprietary Name Detail Record Search

Search results fr m the "Rx" table for query n "020702."

Active Ingredient:	ATORVASTATIN CALCIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	LIPITOR
Applicant:	PFIZER
Strength:	EQ 10MG BASE
Application Number:	020702
Product Number:	001
Approval Date:	DEC 17, 1996
Reference Listed Drug:	No
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	ATORVASTATIN CALCIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	LIPITOR
Applicant:	PFIZER
Strength:	EQ 20MG BASE
Application Number:	020702
Product Number:	002
Approval Date:	DEC 17, 1996
Reference Listed Drug:	No
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	ATORVASTATIN CALCIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	LIPITOR
Applicant:	PFIZER
Strength:	EQ 40MG BASE
Application Number:	020702
Product Number:	003
Approval Date:	DEC 17, 1996
Reference Listed Drug:	No
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

Proprietary Name Detail Record Search

Active Ingredient:	ATORVASTATIN CALCIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	LIPITOR
Applicant:	PFIZER
Strength:	EQ 80MG BASE
Application Number:	020702
Product Number:	004
Approval Date:	APR 07, 2000
Reference Listed Drug:	Yes
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

Thank you for searching the **Electronic Orange Book**

Return to Electronic Orange Book Home Page

Patent and Exclusivity Search Results from query on 020740 001.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020740	001	5006590	JUN 26,2011	
020740	001	5177080	NOV	

Exclusivity Data

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration
020740	001	I-303	JUL 21,2003
020740	001	D-59	JUL 21,2003

Thank you for searching the Electronic Orange Book

Patent and Exclusivity Terms

Return to Electronic Orange Book Home Page

Proprietary Name Search

Proprietary Name Search Results from "Disc" table for query on "baycol."

Appl No	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
020740	CERIVASTATIN SODIUM	Tablet; Oral	0.05MG	BAYCOL	BAYER
020740	CERIVASTATIN SODIUM	Tablet; Oral	0.1MG	BAYCOL	BAYER
020740	CERIVASTATIN SODIUM	Tablet; Oral	0.2MG	BAYCOL	BAYER
020740	CERIVASTATIN SODIUM	Tablet; Oral	0.3MG	BAYCOL	BAYER
020740	CERIVASTATIN SODIUM	Tablet; Oral	0.4MG	BAYCOL	BAYER
020740	CERIVASTATIN SODIUM	Tablet; Oral	0.8MG	BAYCOL	BAYER

Thank you for searching the Electronic Orange Book

Return to Electronic Orange Book Home Page

Proprietary Name Detail Record Search

Search results fr m the "Dis " table for query on "020740."

Active Ingredient:	CERIVASTATIN SODIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	BAYCOL
Applicant:	BAYER
Strength:	0.05MG
Application Number:	020740
Product Number:	001
Approval Date:	JUN 26, 1997
RX/OTC/DISCN:	DISCN

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	CERIVASTATIN SODIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	BAYCOL
Applicant:	BAYER
Strength:	0.1MG
Application Number:	020740
Product Number:	002
Approval Date:	JUN 26, 1997
RX/OTC/DISCN:	DISCN

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	CERIVASTATIN SODIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	BAYCOL
Applicant:	BAYER
Strength:	0.2MG
Application Number:	020740
Product Number:	003
Approval Date:	JUN 26, 1997
RX/OTC/DISCN:	DISCN

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	CERIVASTATIN SODIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	BAYCOL
Applicant:	BAYER
Strength:	0.3MG
Application Number:	020740

Proprietary Name Detail Record Search

Product Number:	004
Approval Date:	JUN 26, 1997
RX/OTC/DISCN:	DISCN
Patent and Exclusivity Info for this product:	Click Here

Active Ingredient:	CERIVASTATIN SODIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	BAYCOL
Applicant:	BAYER
Strength:	0.4MG
Application Number:	020740
Product Number:	005
Approval Date:	MAY 24, 1999
RX/OTC/DISCN:	DISCN
Patent and Exclusivity Info for this product:	Click Here

Active Ingredient:	CERIVASTATIN SODIUM
Dosage Form;Route:	Tablet; Oral
Proprietary Name	BAYCOL
Applicant:	BAYER
Strength:	0.8MG
Application Number:	020740
Product Number:	006
Approval Date:	JUL 24, 2000
RX/OTC/DISCN:	DISCN
Patent and Exclusivity Info for this product:	Click Here

Thank you for searching the **Electronic Orange Book**

Return to Electronic Orange Book Home Page

Patent and Exclusivity Search Results from query on 020702 001.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020702	001	4681893	SEP 24,2009	U-161
020702	001	4681893*PED	MAR	U-161
020702	001	5273995	DEC 28,2010	U-162
020702	001	5273995*PED	JUN 28,2011	U-162
020702	001	5686104	NOV 11,2014	U-213
020702	001	5686104*PED	MAY 11,2015	U-213
020702	001	5969156	JUL 08,2016	
020702	001	5969156*PED	JAN 08,2017	
020702	001	6126971	JAN 19,2013	
020702	001	6126971*PED	JUL 19,2013	

Exclusivity Data

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration
020702	001	I-281	DEC 02,2002
020702	001	D-77	APR 22,2005
020702	001	PED	APR 18,2006
020702	001	I-350	OCT 18,2005
020702	001	PED	JUN 02,2003

Thank you for searching the Electronic Orange Book

Patent and Exclusivity Terms

Return to Electronic Orange Book Home Page